Neurotrophic fungal invasion without a primary focus: Two Rare Cases of Cerebral Chromoblastomycosis in an Immunocompetent Hosts

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Introduction

Chromoblastomycosis is a chronic subcutaneous infection caused by several pigmented fungi such as *Fonsecaea pedrosoi*, *Phialophora verrucosa*, *Fonsecaea compacta*, *Cladophialophora carrionii*, and other species. Cerebral chromoblastomycosis arises from an extracranial infected site and spreads to the brain hematogenously. Revankar *et al.* (SK Shankar1, 2007) in their extensive review of 101 cases of primary CNS pheohyphomycosis found that except for one case with contralateral sinusitis, no patient had sinusitis or otitis making local extension unlikely. The hematogenous route is the most likely source of CNS infection from a primary subclinical pulmonary focus or cutaneous lesions. An intriguing possibility of neurotropism is that of metabolic tropism to melanin that may be responsible for CNS localization. We describe two cases of CNS chromoblastomycosis without any primary skin or lung lesions with different clinical and radiological manifestations.

Aim of the study

To report 2 cases of histologically confirmed pheohyphomycosis, the clinical and radiological profiles.

Methods

Study design: Case Report

Patient selection: patients with histologically confirmed pheohyphomycosis

Parameters recorded: Clinical, radiological, laboratory, treatment given, collected from case records of patients diagnosed as pheohyphomycosis

Case 1: A 17-year-old male presented with sudden onset of slurring of speech and weakness in the left upper limb, followed by weakness in left lower limb On being evaluated elsewhere, and CT brain was suggestive of right capsuloganglionic infract and he was treated conservatively and discharged over the next 48-72 hours he had worsening in sensorium for which he brought to our institute. The rest of history was unremarkable. General physical examination was not significant; vital data were normal. Central nervous system examination sensorium was E3V3M5 with left upper motor neuron type of facial nerve palsy with mild paucity in the left upper and lower limb with bilateral plantar withdrawal. Other system examination was unremarkable. Routine hematological and biochemical investigations were within normal limits. CT brain (Image-1) showed hypodensity in the bilateral capsulo-ganglionic region. MRI Brain plain with contrast (Image-2) showed Acute infarcts in the bilateral thalami, right internal capsule, posterior limb - corticospinal tract, left cerebral peduncle & left gyrus rectus. A few tiny enhancing leptomeningeal nodules are seen along the left uncus, left oculomotor nerve cisternal segment, left MCA cistern & left sylvian fissure. CSF analysis showed 430 cells with 55% lymphocytes and 45% polymorphs with mildly elevated proteins (45mg/dl) and normal glucose, and other meningitis workup was negative. Toxicology screening was negative. Based on CSF analysis and imaging findings, the possibility of meningitis with vasculitis was considered. The patient was started empirically on ATT, ceftriaxone, and Doxycycline. On day 8 of hospital stay, the patient developed GTCS with aspiration pneumonia. The patient was intubated and started on mechanical ventilation. The patient developed fever with decreased sensorium, the antibiotics were escalated, and tracheostomy was done. Other fever workup was negative. Gradually, his fever spikes subsided, and weaning started, and he came out of the ventilator on 24th April. One month into the illness, the repeat MRI (Image 3) was done, which showed temporal evolution of previously seen acute infarcts into chronic infarcts with hydrocephalus and multifocal subacute watershed and left PCA territory infarcts as new findings. Based on this, the possibility of zoster encephalitis was considered, and the patient started on acyclovir, and an MPVP shunt was placed. In due course, he had deranged LFTs, hence modified ATT was given. Repeat CSF showed 26 cells with lymphocyte predominance (24 cells) with normal protein and glucose. Around 10 days later, his fever spikes started to subside, but his sensorium remained status quo. He became unresponsive suddenly, and resuscitation was done as per ACLS guidelines. In spite of all the efforts, he succumbed to the illness on 10/6/23. Consent was obtained for a Clinical autopsy. Clinical autopsy showed Chronic fungal basal meningitis, with Florid Arteritis caused by *Cladosporium cladosporioides,* causing Extensive Ischemic infarcts in the basal ganglia, internal capsule, brainstem, and Extensive laminar necrosis(image-4).

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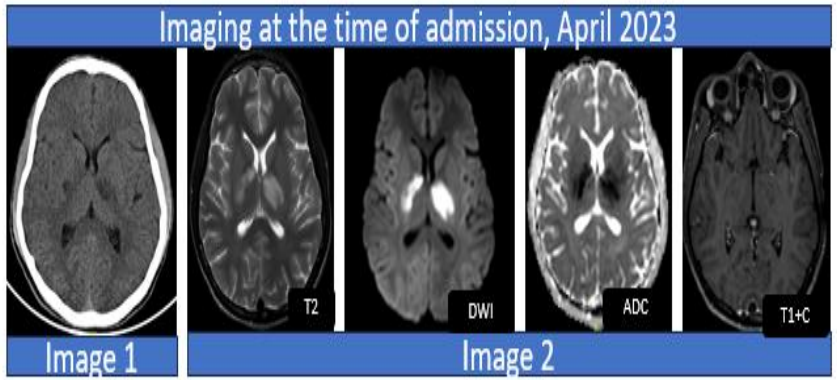
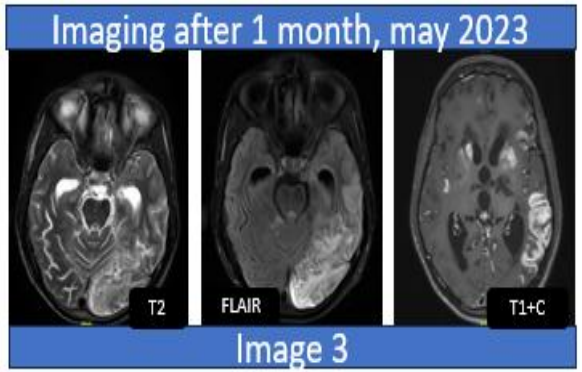
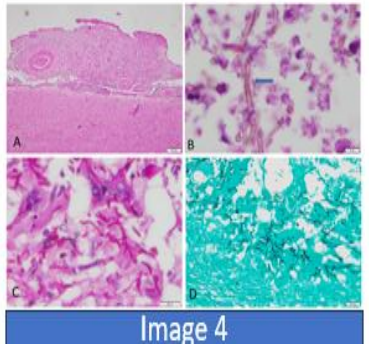






Hematoxylin and Eosin stained sections show dense granulomatous inflammation in the subarachoid space (A)with extension into the underlying neuroparenchyma. Mutiple microabscess formation is seen with central necrotic debris containing pigmented septate fungal hyphae (B). Periodic acid–Schiff stain (C) and Grocott methenamine silver stain (D) highlights the septate fungal hyphae.

Case 2: A 21-year-old male from Bangalore presented with a 20-day history of holocranial headache, acute-onset weakness in the left upper and lower limbs, 7 days of recurrent vomiting, and low-grade fever for 3 days. He had a history of intravenous Thiopentol and cannabis use for the past year. No other significant medical history was noted.

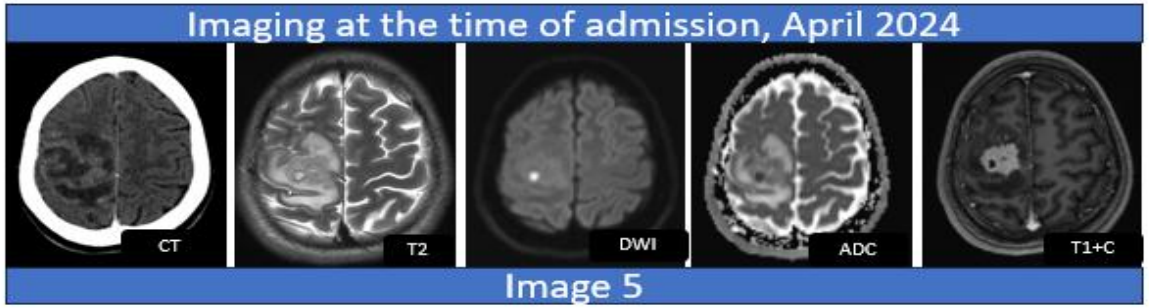
General physical examination was unremarkable, and vital signs were within normal limits. On CNS examination, the patient was conscious, coherent, and oriented. Cranial nerves were intact, except for a left upper motor neuron-type facial nerve palsy. Mild weakness was present in the left upper and lower limbs with an extensor plantar response on the left. Other systemic examination findings were normal.

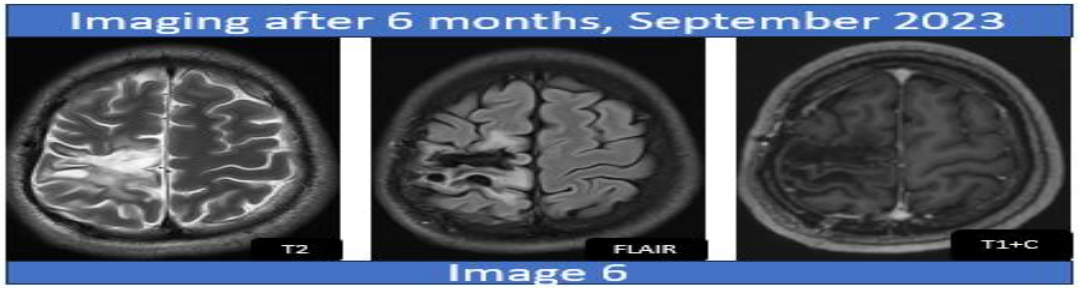
Routine blood investigations were within normal limits. CT brain revealed a hypodense lesion in the right frontoparietal region. MRI brain showed a mixed-intensity lesion on FLAIR and T2-weighted sequences with central diffusion restriction and contrast enhancement (Image 5).

Toxicology screening was negative. A biopsy from the contrast-enhancing lesion in the right rolandic area showed necrotizing granulomatous inflammation with lymphocytes, plasma cells, histiocytes, foamy macrophages, and polymorphonuclear leukocytes. Numerous pigmented, septate fungal hyphae were noted, along with multinucleated giant cells, microabscesses, and dense perivascular inflammation.

Fungal culture grew a dematiaceous fungus identified as *Cladophialophora bantiana*. Gram stain showed a few pus cells with no evidence of bacterial infection, and bacterial cultures were sterile after 48 hours.

A diagnosis of cerebral phaeohyphomycosis was made. The patient was treated with voriconazole and supportive measures. He showed significant improvement in symptoms of raised intracranial pressure and left-sided weakness. Follow-up imaging at 5 months revealed a marked reduction in lesion size with minimal contrast enhancement (image -6).





INCON 2025 KASHI
32nd ANNUAL CONFERENCE OF INDIAN ACADEMY OF NEUROLOGY
29th OCTOBER - 2nd NOVEMBER 2025

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Discussion: These two cases illustrate rare but distinct presentations of CNS chromoblastomycosis, both in immunocompetent hosts and in the absence of primary skin or pulmonary lesions.

Case 1 presented with stroke-like symptoms secondary to fungal arteritis and meningitis, while **Case 2** mimicked a space-occupying lesion with features of a cerebral abscess. CNS involvement without meningitis is uncommon, but abscess formation as a primary manifestation has been described. Conversely, meningitis may also occur as the sole clinical feature.

The frontal lobes are most commonly affected, although other brain regions may be involved. Multiple abscesses can evolve to cause leptomeningitis or ventriculitis. The brown pigmentation of the fungal mycelia is often visible macroscopically. Histologically, the lesions appear as large intraparenchymal abscesses, distinct from the microabscesses seen in *Candida* infections. A granulomatous response is common, often with fungal elements located within giant cells and surrounded by fibrotic tissue and reactive gliosis.

The fungal hyphae are slender (2–3 µm) and show constrictions at regular intervals (every 3–15 µm). In some cases, pigmentation is not apparent with standard stains like PAS or methenamine silver; hence, the melanin-specific Masson-Fontana stain may be necessary to confirm the diagnosis.

Management of primary CNS phaeohyphomycosis is challenging due to limited antifungal efficacy and high mortality, regardless of host immune status. Improved outcomes have been reported with combination therapy using amphotericin B, 5-flucytosine, and itraconazole, though newer agents like voriconazole are also used.

Phaeohyphomycosis remains uncommon in India, with the largest series reported from NIMHANS (14 cases, 7.65%). Most patients presented with frontal lobe abscesses; however, rare presentations such as cerebral infarctions have also been observed. Histological examination typically reveals pigmented fungal hyphae in necrotic abscess walls or infarcted areas. The most frequently isolated organism is *Cladosporium trichoides*. The prognosis is poor, often due to delayed diagnosis, inadequate antifungal therapy, and lack of timely surgical intervention. Early surgical resection combined with antifungal therapy has shown improved survival in some reports (Vyas et al.).

Conclusion: CNS chromoblastomycosis, though rare, can present with diverse and nonspecific clinical and radiological features such as stroke-like symptoms, meningitis, or space-occupying lesions, even in immunocompetent individuals. The absence of a primary cutaneous or pulmonary focus may delay diagnosis. Radiological findings, including infarcts, abscesses, and leptomeningeal nodules, combined with histopathological confirmation, are key to accurate diagnosis. These cases underscore the need for high clinical suspicion and early neuroimaging in atypical presentations. Early histopathological confirmation and timely initiation of antifungal therapy, supported by surgical intervention when appropriate, is crucial to improving outcomes in this otherwise highly fatal condition.